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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,033	11/25/2003	Satoru Miyano	GENN-01009US1	6506

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EXAMINER	
WHALEY, PABLO S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,033	MIYANO ET AL.	
	Examiner	Art Unit	
	Pablo Whaley	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

APPLICANTS' ELECTION

Applicants' election of Group I (Claims 1-17), filed 7/31/2006, is acknowledged. However, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 18-26 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant's election was made without traverse on 7/31/06.

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 1-17.

PRIORITY

Acknowledgment is made of applicant's claim for priority based on provisional application 60/428,827, filed 11/25/2002.

INFORMALITIES

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 16. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-17 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 1-16 are directed to a method for inferring a network relationship between genes, which does not recite either a physical transformation of matter nor a practical application [i.e. concrete, tangible, and useful result]. Instant claim 1 recites steps comprising providing a data library, creating a matrix, generating a set of differential equations, and solving said set of differential equations to produce a network relationship. No description or definition for "providing" data, "creating" a matrix, or "generating" equations is provided in the Specification such that it would be interpreted as a physical steps, therefore the claimed method steps do not result in a physical transformation of matter. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a concrete, tangible, and useful result (i.e. a practical application). However, no actual, concrete result is recited in the claims, nor is any useful result "produced" in a tangible form useful to one skilled in the art.

Claim 17 is directed to a medium containing one or more results of network relationships between genes calculated using the method of claim 1. The "one or more results" of network relationships recited in the claim is non-functional descriptive material. Non-functional descriptive material stored on a medium is not statutory subject matter (e.g. music stored on a compact disk). In the event that applicant intended for said medium to be "computer-readable medium", it is further noted that computer-readable medium encompasses non-physical media, which is not necessarily directed to a physical product, and therefore is also nonstatutory. For

these reasons, the claims are not statutory. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter at 1300 OG 142, Annex IV, Nov. 22, 2005.

LACK OF UTILITY

Claims 1-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well-established utility.

In the instant case, the claimed invention is not supported by a well-established utility. The instant claims generally recite a method for inferring a network relationship between genes. The specification discloses several general disciplines where the development of a gene regulatory network from gene expression data may be "useful" in predicting potential therapeutic targets [p.1] and drug development [p. 2]. Furthermore, the specification discloses several methods for inferring gene networks (i.e. interrelations) from expression data such as clustering algorithms, Bayesian networks, and data modeling using a system of differential equations [p.3, ¶ 3 and p. 4, ¶ 1]. It is noted that instant claim 1 recites "generating a set of linear differential equations" and solving equations to produce said network. However, as instant claim 1 is directly to a method for "inferring a network relationship" this utility is not specific to the instant claims. For these reasons, the claimed subject matter does not have a specific, substantial, and credible utility.

Claims 1-17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted

utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

CLAIM REJECTIONS - 35 USC §112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claims. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below which leads to the determination that the above

claim lacks enablement due to undue experimentation being required to make and use the invention.

In the instant case, the claimed subject matter lacks enablement for the following reasons: Claim 1 is directed to a method for inferring a network relationship between genes requiring (i) providing a quantitative time course data library for a set of genes, (ii) creating a sparse matrix having zero coefficients removed therefrom, (iii) generating a set of linear differential equations, and (iv) solving said set of equations to produce said network relationship. Given the nature of the invention, inferring a network relationship between genes requires inference algorithms to develop an inference model from experimental data such that one skilled in the art would be able to "infer" a network relationship between genes [See 112 2nd rejection below]. However, there are no such limitations recited in the instant claims [Wands factors (2), (4), (8)]. It is noted that instant claim 1, steps (b)-(d) do not necessarily imply the creation of a model and/or modeling of genetic data for inferring a network relationship between genes.

Methods for inferring qualitative relationships in genetic networks from time series data of gene expression patterns are well known in the art [Akutsu et al., Bioinformatics, 2000, Vol. 16, No 8, p.727-734]. Furthermore, methods modeling gene expression data using differential equations and temporal gene expression data are also well known in the art [Chen, Pacific Symposium on Biocomputing, 1999, p.29-40]. Such methods teach the development of inference algorithms, the use of differential equations, techniques for parameter determination (e.g. using linear regression), model specific variables (e.g. mRNA concentrations, protein concentrations, etc.), and the development of qualitative network models for inferring qualitative relationships in genetic networks. It is noted that the instant claims and specification disclose a "sparse matrix" and linear differential equations. However, the specification fails to disclose or provide working examples as to how one skilled in the art would know which parameters and/or

variables to use in the construction of the said "sparse matrix" from a quantitative time course library, as in instant claim 1, step (b). Furthermore, the specification fails to disclose or provide working examples as to how one skilled in the art would be able to infer a network relationship between genes using the said "sparse" matrix and the related linear differential equations as recited in instant claim 1, steps (c) and (d) [Wands factors (2), (3)].

Given the nature of the instantly claimed invention, an inference or network model would need to be developed for modeling gene expression and thereby inferring a network relationship between genes. Sufficient information and guidance is required to develop, test, and validate such an inference model, as supported by the teaching of the prior art, above. Prior art [Akutsu et al., p.733, Col. 1, ¶ 1] also teaches that the application of inference methods to real data are difficult for reasons such as noise, modeling assumptions (e.g. time delays, mRNA concentration data), and biological complexity. Although the level of skill in the art of inferring network relationships from time series gene expression data and modeling gene expression with differential equations is high, as insufficient guidance has been given with regards the development of an inference model for inferring a network relationship, as discussed in detail above, one skilled in the art would require undue experimentation to predictably practice the instantly claimed invention [Wands factors (1), (2), (6), (7)].

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step (a), recites the limitation "providing a quantitative time course data library for a set of genes." It is unclear as to the intended meaning of "a quantitative time course data library " in this context. Clarification is requested.

Claim 1, step (a), recites the "results based on time course of expression of each gene." It is unclear whether "based on" is an actual method step for obtaining said "results", a further limitation of the results, or otherwise. Clarification is requested.

Claim 1, step (a), recites the limitation "said library including expression results...., quantifying an average effect and measure of variability." It is unclear whether said "quantifying an average effect and measure of variability" are intended to be actual method steps directed to averaging and measuring of variability or a further limitations of the said "library." Clarification is requested.

Claim 1, step (b), recites the limitation "creating a sparse matrix." As the specification does not define or fully and completely describe "sparse" for carrying out the intended function, it is unclear as to the metes and bounds intended by applicant for the claimed "sparse matrix" such that one skilled in the art would know which steps creating a "sparse" matrix consists of. Clarification is requested.

Claim 1, step (b), recites the limitation "said matrix having zero coefficients removed therefrom." It is unclear whether said removal step is intended to be an actual method step or a further limitation of the said "matrix." It is noted that there is no previous step directed to the removal of zero coefficients. Clarification is requested.

Claim 4 recites the limitation "the effect of gene j on gene i." As the specification does not define or fully and completely describe "effect" for carrying out the intended function, it is unclear as to the metes and bounds intended by applicant for the claimed "the effect of gene j on gene i" such that one skilled in the art would know what type of effect is intended by the applicant (e.g. up-regulation, down-regulation, intensity, etc.). Clarification is requested.

Claim 6 recites the limitation "said exponent Λt ($\exp(\Lambda)$)." There is lack of antecedent basis for this limitation. There is no basis for this limitation in claim 1. Correction is requested.

Claim 10 recites the limitation "wherein the maximum likelihood estimate of the variance." There is lack of antecedent basis for the "maximum likelihood estimate of the variance." There is no basis for this limitation in claim 1. Correction is requested.

Claim 13 recites the limitation "wherein mask M." There is lack of antecedent basis for this limitation. There is no basis for this limitation in claim 1. Correction is requested.

Claim 17 recites a "medium containing one or more results of network relationships between genes calculated using the method of claim 1." As the specification does not define or fully and completely describe "medium" for carrying out the intended function, and as the specification also disclose an "MMGE medium" [p.12 and 15], it is unclear as to the metes and bounds intended by applicant for the claimed "medium" such that one skilled in the art would know which steps this consists of. Clarification is requested.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP §

2172.01. Claim 1 recite methods for "inferring a network relationship between genes" in the preamble. The omitted essential steps appear to be between steps (a) and (d) since the instant claims do not indicate which steps would indicate inferring a network relationship between genes. Moreover, it is unclear in what way one would arrive at an inferred relationship between the data, since no model or algorithms are provided for inferring qualitative relationships between genes. Clarification is requested. Claims 2-3, 5, 7, 8-9 and 11, 12, and 14-16 are rejected as they depend directly or indirectly from claims 1, 4, 6, 10, and 13.

CLAIM REJECTIONS - 35 USC § 102

It is noted that because the claims recite the limitation "sparse matrix" which is indefinite (see 112, 2nd), the Examiner has interpreted the claims broadly. Therefore, the following prior art rejection is applicable.

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102 (b) as being anticipated by Chen [Pacific Symposium on Biocomputing, 1999, p.29-40].

Chen teaches methods for modeling gene expression data using differential equations and temporal gene expression data. More specifically, Chen teaches the following aspects of the instantly claimed invention:

- Providing time series mRNA and protein concentration data [p.32], as in instant claim 1.
- Creating a non-singular diagonal matrices and generating a set of linear differential equations [p.33, lines 1-13], as in instant claims 1 and 3.
- Solutions to the linear differential equations [p.33, lines 14-19], as in instant claim 1.

CONCLUSION

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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9/18/06